REMARKS

In an Office Action dated September 7, 2004, claims 1, 3-6, 8, 10-20, 47, and 48 of the claims under consideration in the subject patent application, were rejected. Claim 9 was allowed and claims 2, 4, 7, and 10 were objected to. By amendment above, claims 1, 4, 7, 10, and 15 have been rewritten. Support for the amendments in claims 1 and 4 can be found on page 3 of the specification. Support for the amendments in clam 10 can be found in original claims 10 as filed in the original German patent application. A typographical error has been corrected in claim 15, claiming dependency from claim 14 which claim provides proper antecedent basis and not claim 13.

Reconsideration of this application and allowance of the claims is respectfully requested in view of the foregoing amendments and the following remarks.

The Examiner has objected to claims 4 and 10. According to the Examiner the R groups denoting isocyanate and isothiocyanate groups should be deleted because these groups have been deleted from independent claim 1. Applicants submit that claims 4 and 10 as amended no longer contain R groups denoting isocyanate and isothiocyanate groups. Therefore, applicants respectfully request withdrawal of the objection.

The Examiner has rejected claims 1, 3-6, 8, and 10-19 in the pending application as anticipated by Hogan et al (WO97/18226). According to the Examiner, Hogan et al discloses immobilization of biopolymers on a solid phase comprising a solid phase which contains an epoxide which can react with amino groups and which can react with a biopolymer comprising a reactive group. The Examiner further asserts that Hogan et al discloses an hybridization device comprising an oligonucleotide probe, and a solid substrate, whereby the solid substrate has a

support surface with a neutral or negative electrostatic field and a hybridization surface accessible for linking an oligonucleotide probe with such solid substrate at a distance of no more than about 100 angstoms. Further, according to the Examiner, Example 12 in Hogan et al shows that the -NH2 group is linked at the 3' terminal of the nucleic acid. The Examiner also asserts that specific embodiments includes methods for detecting single base differences in a target area of a strand of DNA or RNA comprising mixing a hybridization device with DNA or RNA containing the target area to be detected; allowing hybridization; altering the environment of the hybridization probe and DNA or RNA target area to remove non-hybridized DNA or RNA; and detecting the DNA or RNA hybridized to the hybridization device.

Applicants submit that claim 1, as amended, and dependent claims thereon are not directed to epoxides as surface reactive groups on a glass surface. Furthermore, there is no indication in Hogan et al with respect to the use of halogenide or aldehyde modified surfaces. Thus the solid phase as prepared by the claimed invention as amended differs from the solid phase as taught by Hogan et al. Therefore, claim 1 and dependent claims 3-6, 8, and 10-19 are not anticipated by Hogan et al. Accordingly, withdrawal of the rejection is respectfully requested.

The Examiner has rejected claims 20, 47 and 48 as obvious over Hogan et al (WO97/18226) in view of Lipshutz et al (Biotechniques Vol. 19, No.3, 1995, pp 442-447). According to the Examiner Hogan et al discloses immobilization of biopolymers on a solid phase, the solid phase containing an epoxide which can react with amino groups and which can react with a biopolymer comprising a reactive amino group, and Lipshutz describes using oligonucleotide probe arrays to access genetic diversity. The Examiner asserts that therefore it would have been obvious to use the method of Hogan et al for the determination of gene

expression since Lipshutz discloses that oligonucleotide probe arrays display specific oligonucleotide probes at precise locations in a high density, information rich format. This, according to the Examiner, can be applied to a broad range of nucleic sequence analysis problems including pathogen identification, polymorphism detection, human identification, mRNA expression monitoring and de novo sequencing, as described in Lipshutz.

In response to the Examiner's assertions, the presently claimed invention, as amended, is not obvious over Hogan et al. in view of Lipshutz et al because, contrary to the Examiner's assertions, Hogan et al. does not disclose the immobilization of biopolymers on a solid phase according to claim 1, as amended. Although Hogan et al. discloses the immobilization of biopolymers on a solid phase, the solid phase of the present invention is very different from the solid phase of Hogan et al. In particular there is no indication in Hogan et al. to use the halogenide or aldehyde modified surface as in the present invention. This deficiency is not cured by Lipshutz et al. Moreover, Lipshutz et al describes the principle of oligonucleotide probe arrays, manufactured by Affymetrix, and their use for a broad range of nucleic acid sequence analysis applications, including mRNA expression monitoring. The arrays in Lipshutz et al are prepared by means of a stepwise synthesis of the oligonucleotides on the surface of the array. In contrast, the present invention describes methods for preparing arrays from already prepared biopolymers which are immobilized on a solid surface. The arrays in Lipshutz et al are limited to contain oligonucleotides of a certain length. See Lipshutz et al on page 443, middle column last paragraph and right column, second paragraph. This limitation on the length of the oligonucleotides in Lipshutz et al is to limit impurities in the oligonucleotides and the content of undesired by-products. Furthermore, the by-products of this method of synthesis cannot be

removed. Therefore, the genetic information contained in these arrays is limited in view of these factors. In contrast, the pre-formed oligonucleotides of the present invention can be synthesized in much longer sequences, i.e. at least 100 bases, and in much higher purity, as by-products can be removed. For this reason the present invention may have broader applications and has superior properties such as better hybridization efficiency, resulting in higher signals, higher quality data, less sample input required and higher gene-specificity. Also the density of the array in Lipshutz et al may decrease accessibility of the sample to the oligonucleotides which may require different approaches to sample preparations, such as partial digestion. These can be time consuming and may result in altered signal/information output, increasing the percentage of false positives and negatives. Furthermore, in contrast to the present invention, the oligonucleotides in Lipshutz et al cannot be removed from the support. Thus the array of Lipshutz et al cannot be reused. Thus the method of the present invention is distinctly different from the method of Lipshutz et al. The use of pre-formed oligonucleotides to form immobilized oligonucleotides results in an improved, more precise and more efficient determination of gene expression, gene function and metabolism. In addition, Hogan et al do not teach or suggest the array of the present invention as described. Therefore, the combination of Hogan et al with Lipshutz et al does not teach or suggest the method in claim 20, 47 and 48 of the present invention. At most there is a suggestion to try. However, a suggestion to try without a reasonable expectation of success does not render obvious the methods of the present invention. Therefore, applicants submit the presently claimed invention in claims 20, 47, and 48 is not obvious over Hogan et al in view of Lipshutz et al. Accordingly, withdrawal of the rejection is respectfully requested.

The Examiner also objected to claims 2 and 7 as being dependent upon a rejected base claim, but indicated that claims 2 and 7 would be allowable if rewritten in independent form

including all of the limitations of the base claim and any intervening claims. Applicants have incorporated all the limitations of claim 1 and intervening claims 5 and 6 into claim 7. Therefore, applicants submit claim 7 is allowable in light of the Examiner's statement. Accordingly, applicants respectfully request withdrawal of the objection to claim 7. Further, with respect to claim 2, applicants submit that claim 1, as amended, is not anticipated by Hogan et al as discussed above. Claim 2 is a further limitation of claim 1 with respect to the functional groups on the solid substrate of claim 1. Therefore, applicants submit that claim 2 is allowable in view of claim 1, as amended, and the Examiner's statement. Withdrawal of the objection to claim 2 is respectfully requested.

Further, applicants appreciate and acknowledge the Examiner's allowance of claim 9. Applicants submit that the present application is now in condition for allowance.

Reconsideration and favorable action are earnestly requested.

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